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Effects of artificial dawn on sleep inertia, skin temperature, and the awakening cortisol response

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SUMMARY The effect of artificial dawn during the last 30 min of sleep on subsequent dissipation of sleep inertia was investigated, including possible involvement of cortisol and thermo-regulatory processes. Sixteen healthy subjects who reported difficulty with waking up participated in random order in a control and an artificial dawn night. Sleep inertia severity was measured by subjective ratings of sleepiness and activation, and by performance on an addition and a reaction time task measured at 1, 15, 30, 45, 60, and 90 min after waking up at habitual wake up time at workdays. At all intervals, saliva samples were collected for cortisol analysis. Sleep electroencephalogram was recorded during the 30 min prior to waking up; core body temperature and skin temperatures were recorded continuously until 90 min after waking up. Subjective sleepiness was significantly decreased and subjective activation increased after waking up in the artificial dawn condition as compared with control, in which lights were turned on at waking up. These effects can be explained by effects of artificial dawn on skin temperature and amount of wakefulness during the 30 min prior to the alarm. Artificial dawn accelerated the decline in skin temperature and in the distal-to-proximal skin temperature gradient after getting up. No significant effects of artificial dawn on performance, core body temperature, and cortisol were found. These results suggest that the physiology underlying the positive effects of artificial dawn on the dissipation of sleep inertia involves light sleep and an accelerated skin temperature decline after awakening.

KEYWORDS artificial dawn, cortisol, human, light, skin temperature, sleep inertia

INTRODUCTION

During the period immediately after waking up people may suffer from confusion, disorientation, sleepiness and grogginess, and cognitive and physical performances may not be optimal. This transitory process is called sleep inertia (Dinges, 1990; Kleitman, 1963; Tassi and Muzet, 2000). The severity and

duration of sleep inertia vary because of variations in sleep architecture, sleep stage upon awakening, and circadian phase (Scheer *et al.*, 2008; Tassi and Muzet, 2000). Under natural situations sleep inertia generates risks, in particular when performance immediately upon awakening must be high, for example when participating in traffic (Dinges and Kribbs, 1991; Seminara and Shavelson, 1969). It is of great interest for individuals and for society to understand the processes involved in waking up and to test methods to reduce sleep inertia. One of these methods is tested in this study, which experimentally addresses the effects of artificial dawn prior to waking up.

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Sleep inertia is seen upon awakening from various sleep durations (Brooks and Lack, 2006; Jewett *et al.*, 1999), and at all times of day and night (Naitoh *et al.*, 1993; Wilkinson and Stretton, 1971). Immediately after waking up, sleep inertia complaints are largest (Seminara and Shavelson, 1969). In the first hour after awakening, subjective alertness and cognitive performance rapidly improve, and sleep inertia slowly dissipates in an asymptotic manner (Jewett *et al.*, 1999).

The severity of sleep inertia is mainly assessed by its intensity and duration (Tassi and Muzet, 2000). Reported durations of sleep inertia vary from several minutes (Wilkinson and Stretton, 1971) up to several hours (Naitoh, 1981). This large variation can be a consequence of the applied types of tests, for example, with high and low cognitive load, or the methods of analysis (Achermann *et al.*, 1995; Ferrara and De Gennaro, 2000; Jewett *et al.*, 1999; Muzet *et al.*, 1995). Sleep inertia is influenced by preceding sleep and can be quite severe. After 8 h of normal sleep, the effects of sleep inertia are reported to be modest and short-lived (Achermann *et al.*, 1995; Jewett *et al.*, 1999), nevertheless cognitive performance immediately after waking up is worse than after a night of total sleep deprivation (Wertz *et al.*, 2006).

Especially late chronotypes suffer from sleep inertia on a daily basis (Roenneberg *et al.*, 2003); because of the demands of society they show a large discrepancy between obligatory and preferred timing of sleep (Horne and Östberg, 1976; Roenneberg *et al.*, 2003; Zavada *et al.*, 2005), resulting in so-called social jetlag (Wittmann *et al.*, 2006). The increased severity of sleep inertia of late chronotypes compared with early chronotypes may originate from three sources. First, their circadian phase in the morning is not optimal for high performance. Second, sleep duration during workdays is short because of late sleep onset and early wake up. Recovery sleep after partial or total sleep deprivation is known to increase the severity of sleep inertia (Balkin and Badia, 1988), possibly due to increased amounts of slow-wave sleep (SWS; deep sleep) or to an increased chance of waking up from SWS (Dinges, 1990). Third, being sleepy in the morning motivates to get out of bed as late as possible, shifting the interval of severe sleep inertia to a period with high performance demands like commuting.

In this study, we test if artificial dawn reduces the severity of sleep inertia in people who report having difficulty getting up in the morning on workdays. We also investigate possible physiological correlates of the induced effects. The process of waking up in the morning coincides with a wide range of physiological changes, among which changes in electroencephalogram (EEG) spectrum (Tassi *et al.*, 2006), thermoregulatory changes (Kräuchi *et al.*, 2004) and changes in cortisol level (Aschoff, 1978). These changes might be associated with the dissipation of sleep inertia. Changes in the distal-to-proximal skin temperature gradient (DPG) have been shown to correlate with sleepiness immediately after waking up (Kräuchi *et al.*, 2004). Cortisol starts to increase during the second half of the night and is typically characterized by peak levels shortly after awakening (Edwards *et al.*, 2001; Wüst *et al.*, 2000). Waking up during the peak of the cortisol

rhythm results in a short-lasting further elevation of the cortisol level (Edwards *et al.*, 2001; Hucklebridge *et al.*, 2005; Wüst *et al.*, 2000); this elevation is called the awakening cortisol response. Elevated plasma cortisol levels during the second half of the night have been associated with an increase in stage 1 sleep, movements, and wakefulness, supporting an awakening effect of cortisol (Born *et al.*, 1986; Fehm *et al.*, 1986). This was confirmed experimentally by direct administration of cortisol during sleep (Born *et al.*, 1989). Whether the awakening cortisol response is related to sleep inertia complaints is not known.

Light plays an important role in alerting the body (Cajochen *et al.*, 2000; Rüger *et al.*, 2003), both during the day and during the night (Phipps-Nelson *et al.*, 2003; Rüger *et al.*, 2006). Furthermore, bright light after waking up in the morning has been shown to increase cortisol levels in healthy humans while light at other times of the day does not (Leprout *et al.*, 2001; Rüger *et al.*, 2006; Scheer and Buijs, 1999).

Few studies test the effects of a dawn light signal in the early morning on physiological and psychological parameters. Dawn simulation that started during sleep increased the awakening cortisol response (Thorn *et al.*, 2004) and improved sleep quality (Leppämäki *et al.*, 2003) in healthy individuals. A dawn signal has been shown to decrease depressive symptoms in seasonal affective disorders (SAD; Avery *et al.*, 1993, 2001; Terman *et al.*, 1989), and has been shown to be effective in decreasing sleep inertia in patients with SAD and subsyndromal SAD (Avery *et al.*, 2002; Norden and Avery, 1993). Dawn-dusk simulation light therapy has been shown to improve sleep quality and to advance sleep timing in demented elderly (Gasio *et al.*, 2003).

This lab study involved two conditions in which only the dawn period during the last 30 min of sleep was manipulated. A condition with artificial dawn during sleep and light at waking up was compared with a condition with light at waking up only. The purpose of this experiment was to investigate the effect of artificial dawn during sleep on sleep inertia and physiological processes in people who regularly have to wake up earlier than desired. Three aspects were investigated: sleep architecture during the stimulus; body (core and skin) temperature regulation; and cortisol production immediately after waking up, in relation to sleepiness, activation, stress, and performance measures.

MATERIALS AND METHODS

Subjects

Subjects were recruited by advertisements in public places and at the University of Groningen. Sixteen healthy subjects [eight men and eight women, mean age (\pm SD) 22.8 ± 4.6 years] were selected, based on the following criteria: subjects had to be between 18- and 36-years old, and live a regular life that consisted of at least four working days a week. On these days, they had to report that they need at least 60 min to fully wake up in the morning [rated on the Munich Chronotype

Questionnaire (MCTQ; Roenneberg *et al.*, 2003]. This selection resulted in relatively late chronotypes: mean midsleep on free days (MSF) (\pm SD) $5:53 \pm 64$ min (range from the same age categories, mean MSF 4:25–5:23, Dutch population; Zavada *et al.*, 2005), who also had a relatively large 'social jetlag' mean (\pm SD), 1.88 ± 0.82 h (Wittmann *et al.*, 2006). To obtain a marker for circadian phase, MSF corrected for sleep deficit accumulated over the workweek (Roenneberg *et al.*, 2007) was calculated: mean MSFsc (\pm SD) $5:23 \pm 64$ min. Other subject characteristics (mean \pm SD) were: timing of lights off on workdays $23:48 \pm 53$ min; timing of alarm on workdays $7:53 \pm 54$ min; time needed to fully wake up on workdays 1.75 ± 0.87 h; phase angle between MSFsc and start of artificial dawn 1.99 ± 0.76 h (range 0.77–3.43 h). Subjects were healthy, did not suffer from (winter) depression (Beck Depression Inventory-II, Dutch version, BDI-II_NL ≤ 8 ; Beck *et al.*, 1996, 2002) or sleep disorders, and did not use medication including sedatives, except for oral contraceptives (three women), NuvaRing® (Organon, Oss, The Netherlands) (one woman), hormone spiral (one woman) and copper spiral (one woman). Shift workers and persons who had experienced transmeridian flights within the last month were excluded from the study. All subjects were born and raised in The Netherlands so that they were fully able to understand the Dutch questionnaires. All subjects gave written informed consent and were paid for their participation. The experimental protocol was approved by the Medical Ethics Committee of the University Medical Center Groningen.

Subjects were asked to keep a sleep–wake schedule for workdays during the 7 days at home prior to participation, and to take no naps during the experimental days. In most cases, subjects would participate on the same day of the week in the control and artificial dawn condition (maximum difference 2 days). Drinking coffee or alcohol on the days of participation was not allowed. All subjects reported to have kept to this regime.

Experimental design

Subjects came to the human time isolation facility of the Department of Chronobiology at the University of Groningen on two occasions (control condition and experimental condition; Fig. 1), consisting of two nights each. Subjects were free to go home during the day in between. Subjects stayed in individual living and bedrooms with no information about time of day. All rooms were completely dark, without windows. The living room was lit by ceiling lighting resulting in an intensity of 300 lux measured at eye level in the direction of the computer screen. During all four nights of the experiment subjects slept according to their habitual sleep time on workdays.

Condition order was randomized, and there was a minimum of 1 week between conditions. The first night of each condition served as an adaptation night, which was not followed by a testing period in the morning, and subjects were allowed to leave after breakfast. The second night was either the control or experimental night, followed by a testing period of 90 min

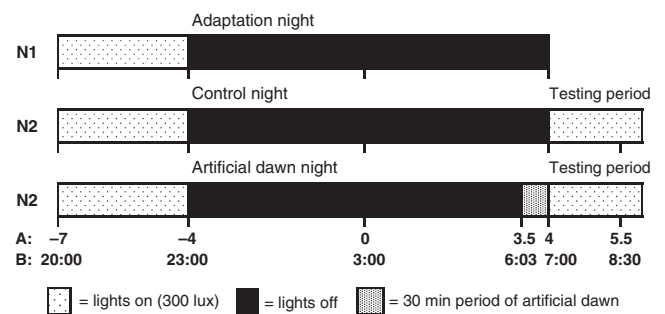


Figure 1. Scheme of the experimental design. Subjects arrived 3 h before habitual bedtime. All tests and questionnaires were made twice during this period to get familiar to them. The first night (N1) served as an adaptation night. The second night (N2) was either the control night or the experimental night, which ended in a 30-min period of artificial dawn. The first test session started 1 min after waking up, the last test session started 90 min after waking up. (A) Relative time to habitual midsleep on workdays (h). (B) Accompanying example if habitual sleep time on workdays is from 23:00 to 07:00 hours.

after which subjects were allowed to leave. Adaptation and control nights did not have a period of artificial dawn prior to wake up, instead, simultaneously with the audible alarm, the light was switched on with an intensity of 300 lux, measured at eye level in the direction of the Wake-up Light at 40 cm distance (the Wake-up Light is modified in such a way that no period of artificial dawn preceded the alarm; Philips DAP B.V., Drachten, The Netherlands). The experimental night was concluded with a 30-min period of artificial dawn, in which the light increased (up to the maximum of 300 lux) before the alarm and remained on after the audible alarm (normal Wake-up Light; Fig. 5). Two Wake-up Lights were used, placed on either side of the bed to make sure that the subjects were exposed to the light. The Wake-up Light uses a 105-W light bulb (HalogenA Pro, Philips Lighting, Eindhoven, The Netherlands). Each night was ended by an audible alarm at the habitual wake up time, which made a ticking sound. At the same moment, a researcher entered the room to make sure that the subjects got out of bed immediately. They subsequently walked to their individual living room and stayed seated behind the computer for the 90-min testing period. They were allowed to visit the toilet once preferably between 15 and 30 min after the audible alarm. All recordings were carried out between 16 January and 15 March 2007.

Measurements

Sleep inertia: subjective ratings and performance

All questionnaires and performance tasks were practiced twice on each of the four evenings in the lab. Subjective ratings of sleepiness [Karolinska Sleepiness Scale (KSS); Åkerstedt and Gillberg, 1990] were obtained at 1, 15, 30, 45, 60, and 90 min after the alarm. Ratings on the KSS range from 1 to 9, with 1 meaning very alert and 9 meaning very sleepy. Subjective ratings of activation and stress (two factors of the Thayer Adjective check list; Thayer, 1967), with ratings ranging from

10 = minimal up to 40 = maximal, were obtained 1, 30, 60 and 90 min after the alarm. At 1, 30, 60, and 90 min after the alarm two performance tasks were conducted. The first one was an addition task in which subjects were asked to make as many correct additions as possible within a 3-min period. All additions consisted of two numbers of two digits. The second task was a simple reaction time task in which during 2 min, 30 stimuli were presented with varying intervals. Subjects had to respond by pressing the spacebar as quickly as possible. For the calculation of the average reaction time, lapses (response time > 500 ms) and anticipatory responses (response < 150 ms) were excluded.

Body temperature

Core body and skin temperatures were recorded throughout the night at a rate of one sample per minute. Recording ended immediately after the alarm following the adaptation nights, and after the last testing periods following the control and experimental night. Core body temperature was measured continuously by a rectal probe and recorded with the online wireless recording Puck Temperature Telemetry system (Ambulatory Monitoring, Ardsley NY, USA). Skin temperature was measured using Ibuttons (DS1922L, Maxim Integrated Products, Sunnyvale, CA, USA; resolution 0.0625 °C; for validation, see Marken Lichtenbelt *et al.*, 2006) that were placed on 11 locations: both hands (ventral part of left and right wrist) and both feet (inner part of left and right foot, just below the ankle bone); left and right infraclavicular region; inner part of left and right thigh; inner part of left and right calf; and one on the sternum. For the analysis distal skin temperature was calculated by averaging the skin temperature of both hands and feet, and proximal skin temperature was calculated as the average temperature of the left and right thigh, left and right infraclavicular region, and sternum using the following formula (see Mitchell and Wyndham, 1969):

$$\text{Proximal skin temperature} = \frac{\text{average thigh} + (\text{average infraclavicular region} + \text{sternum})}{2}$$

The data from the calf were excluded in calculating proximal skin temperature because they appeared to represent intermediate values between those from distal and proximal locations. The DPG was calculated as the difference between distal minus proximal skin temperatures.

Only the last 30 min of sleep until 90 min after the alarm will be compared between conditions for core body and skin temperature. One male subject had to be excluded from the analysis of skin temperature because data of some skin temperature locations were missing.

Cortisol

Saliva samples for cortisol analysis were taken at 1, 15, 30, 45, 60 and 90 min after the alarm, using Salivettes® with a cotton

swab (Sarstedt B.V. Etten-Leur, The Netherlands). During the 90 min, eating and drinking (other than water) were not allowed. A coated tube radioimmunoassay cortisol kit was used to determine cortisol levels (Spectria, Orion Diagnostica, Espoo, Finland). Each series from one individual was analyzed within the same assay; sensitivity: 0.19 nmol L⁻¹ (lower limit); intra- and inter-assay variations: 3.9 and 6.7%, respectively.

Sleep EEG

Sleep EEGs were recorded during all four nights. EEG derivations consisted of C3-A2, Fz-A1, in addition to two electrooculogram (eye movements) and two electromyogram (EMG; muscle tone) electrodes. The EEG recordings were low-pass filtered at 30 Hz (24 dB oct⁻¹) and digitized at a sample rate of 128 Hz. Sleep stages were visually scored on 30-s epochs according to the criteria defined by Rechtschaffen and Kales (1968). For the present purpose, only the last half hours of sleep in the control condition and the artificial dawn condition were analyzed.

Statistical analysis

The differences over time of subjective ratings of sleepiness, activation, stress and performance on an addition and reaction time task were tested with a repeated-measures ANOVA, with two within factors (time and condition). The first measurement after waking up was tested separately to check whether already at this moment a difference could be observed between the control and artificial dawn condition. Similar statistics was used to test the pattern of cortisol concentration over time.

To determine the effects of light condition on core body, distal skin, proximal skin and DPG temperature profiles, mixed effect regression analysis (also known as hierarchical or multilevel analysis) were applied using MLwiN software (Centre for Multilevel Modelling, Institute of Education, London, UK). These analyses take into account the interdependency of the data points inherent to the hierarchical structure of the design, in our case the 1-min interval sequential temperature measurements *i* that were nested within days *j*, once more nested within participants *k* (Twisk, 2003). Moreover, the software package allows for the definition of an autocorrelated residual error data structure, which cannot be neglected in frequently sampled temperature values. After observation of the temperature curves and based on our hypothesis, the following model equation was used to fit the data:

$$\begin{aligned} \text{Temperature}_{ijk} = & \beta_{0ijk} + \beta_1 \times \text{Dawn}_{ijk} + \beta_2 \times \text{tpost}_{ijk} \\ & + \beta_3 \times \text{Sqrt}(\text{tpost})_{ijk} + \beta_4 \times \text{Dawn} \times \text{tpost}_{ijk} \\ & + \beta_5 \times \text{Wakefulness}_{ijk} + \beta_6 \times \text{Wakefulness} \\ & \times \text{tpost}_{ijk} \end{aligned}$$

where β_0 represents the model intercept, β_1 the main effect of the artificial dawn condition (Dawn) as present from the start

of dawn signal to the end of the 90-min postalarm period, β_2 and β_3 together represent the non-linear time course of the decline in temperature after getting up (tpost indicates the time since getting up), β_4 the linearly increasing difference between the artificial dawn and control temperature time courses after getting up, β_5 the main effect of the amount of wakefulness during the 30 min prior to the audible alarm, and β_6 the effect of wakefulness prior to the alarm on the rate of decline of temperature after getting up. Parameters β_1 describe the main (time-independent) effect of artificial dawn, and β_4 its accelerating effect on the decline in temperatures after getting up. The autocorrelation of residual errors was included in the model as an exponentially decaying function of the time interval between successive temperature measurements. Maximum likelihood was used to estimate the regression coefficients, which were tested for significance with the *z*-test.

To determine if cortisol concentration during the period of artificial dawn is already influenced, the difference in cortisol concentration at 1 min after waking up was analyzed first, using a paired samples *t*-test. The effect of artificial dawn over time was analyzed using repeated-measures ANOVA (both the whole 90 min and the first 30 min based on the results found by Thorn *et al.*, 2004). The highest peak during the 90 min after waking up was analyzed using a paired samples *t*-test, and the difference in the timing of the highest peak in cortisol concentration was analyzed using a 'sign' test. For graphical purposes only (Fig. 4), cortisol samples were normalized as follows: all samples per subject were divided by the average of all samples over both conditions of that subject and then multiplied by 100%.

The differences between conditions for percentages of sleep stages, sleep efficiency, first arousal, accumulation of wakefulness, and final wake up time were tested with the Wilcoxon matched-pairs signed rank test, and the difference in sleep stage on final awakening with a chi-square test.

A mixed effect multiple regression analysis (MLwiN software) was used to determine whether sleepiness and activation scores could be predicted (other than by the time since alarm, dawn and their interaction) by the physiological parameters 'momentary temperature' (core, distal, proximal, DPG), 'momentary cortisol' and 'wake/sleep stage duration during the final 30 min prior to the alarm' [movement time, W, S1–4, rapid eye movement (REM)]. To determine if circadian phase could explain sleepiness and activation scores, the phase angle between MSFsc and start of artificial dawn was added to the model. To investigate whether artificial dawn had a differential effect on sleepiness and activation depending on circadian phase, the interaction between dawn and circadian phase was tested. By the use of the $-2 \times \log$ likelihood the most parsimonious model was selected using backward selection. Ancillary analyses using forward selection led to identical results. The significance of regression coefficients was tested with the *z*-test.

Values are described as average \pm SEM. All tests are performed with $\alpha = 0.05$, two-tailed.

RESULTS

Subjective ratings and performance

Sleepiness (KSS) was highest shortly after waking up and decreased significantly during the following 90 min (Fig. 2a; $F_{5,11} = 14.11$, $P < 0.001$), whereas subjective ratings of activation (Thayer-activation) showed the opposite pattern (Fig. 2b; $F_{3,13} = 21.03$, $P < 0.001$). Significantly lower levels of sleepiness ($F_{1,15} = 4.58$, $P < 0.05$) and higher levels of subjective activity ($F_{1,15} = 7.58$, $P < 0.02$) were found in the 90 min after artificial dawn compared with the same period in the control condition. At the first time point after waking up, neither sleepiness nor activation differed significantly between the artificial dawn and control condition (sleepiness: $F_{1,15} = 0.32$, NS; activation: $F_{1,15} = 3.09$, NS). There was no significant interaction between condition and time, neither for sleepiness ($F_{5,11} = 1.44$, NS) nor for activation

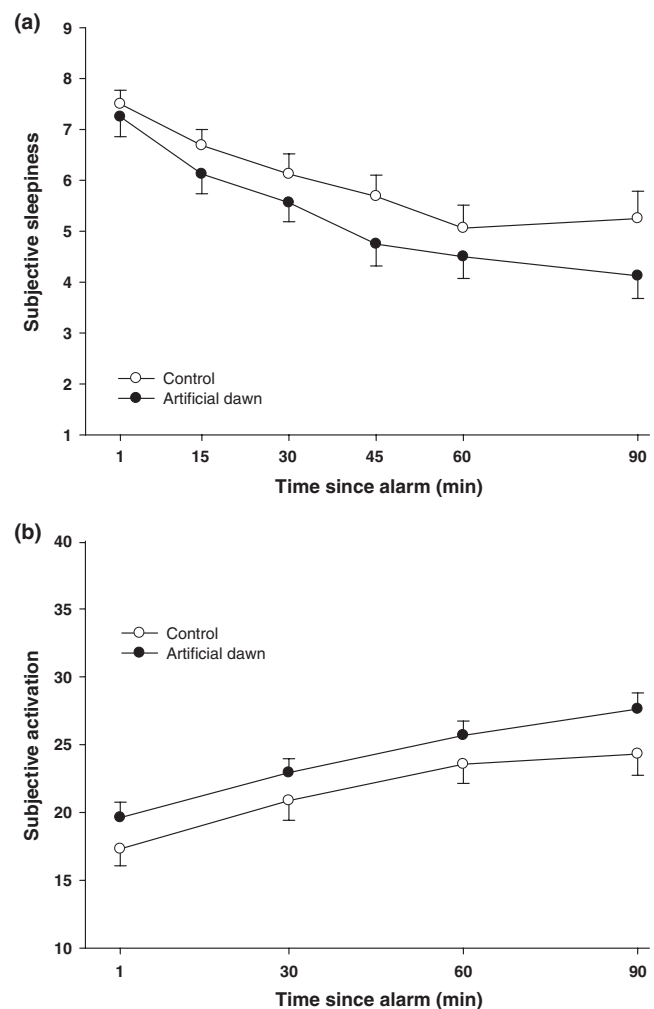


Figure 2. Average (\pm SEM) subjective ratings in the control (open symbols) and artificial dawn conditions (closed symbols) during the 90 min after the audible alarm for: (a) Sleepiness (KSS, 1 = low and 9 = high sleepiness); (b) Activation (Thayer Adjective check list, 10 = low and 40 = high activation) ($n = 16$).

($F_{3,13} = 0.79$, NS), meaning that there was no significant deceleration/acceleration of sleepiness and activation after waking up between conditions. The subjective stress levels (Thayer-stress) were very low (data not shown) and there was no significant difference in pattern over time ($F_{3,13} = 3.33$, NS). No significant main effect ($F_{1,15} = 3.07$, NS) or interaction effect ($F_{3,13} = 1.63$, NS) over time was found between conditions. The first stress rating after waking up did not differ between the artificial dawn and control condition ($F_{1,15} = 0.08$, NS).

Performance was measured by addition and simple reaction time tasks. On the addition task, both the number of correct additions and the total number of additions increased over the 90-min wake time after the audible alarm. The number of correct additions at 1 min after waking up increased from 35.6 ± 2.3 to 43.2 ± 2.0 at 90 min after waking up ($F_{3,13} = 9.21$, $P < 0.01$), and the total number of additions increased from 37.0 ± 2.3 to 44.3 ± 2.1 ($F_{3,13} = 12.73$, $P < 0.001$) with no significant differences between conditions (correct additions: $F_{1,15} = 0.11$, NS; total additions: $F_{1,15} = 0.16$, NS) and no significant interaction between condition and time (correct additions: $F_{3,13} = 1.55$, NS; total additions: $F_{3,13} = 1.09$, NS). At the first time point after waking up, neither number of correct additions nor total number of additions differed significantly between the artificial dawn and control condition (correct additions: $F_{3,13} = 0.55$, NS; total additions: $F_{1,15} = 0.49$, NS).

On the simple reaction time task, a significant reduction in reaction time over time was found (average reaction time 1 min after waking up: 270.5 ± 5.0 ms, decreasing to 258.4 ± 3.7 ms at 90 min after waking up, $F_{3,13} = 8.08$, $P < 0.01$), but no significant differences were found between conditions ($F_{1,15} = 1.37$, NS), nor was there a significant interaction effect between condition and time ($F_{3,13} = 0.66$, NS). The first measurement after waking up did not differ between the artificial dawn and control condition ($F_{1,15} = 0.00$, NS).

Skin and core body temperatures

As shown in Fig. 3, the artificial dawn condition did not significantly affect temperatures while still in bed, but did accelerate the decline in distal and proximal skin temperature, and their difference, after getting up. The mixed effect regression model fitted the time course of the temperature measures well, and confirmed that there were no significant main effects of artificial dawn on distal temperature (β_1 estimate = -0.06 ± 0.15 °C, NS), proximal temperature (-0.15 ± 0.13 °C, NS), DPG (0.10 ± 0.14 °C, NS) or core body temperature (-0.11 ± 0.07 °C, NS). In contrast, artificial dawn significantly accelerated the decline in skin temperatures after getting up, most strongly so for distal temperature (β_4 estimate = -0.36 ± 0.04 °C h⁻¹, $P < 0.0001$), less prominent but still significant for proximal temperature (-0.07 ± 0.03 °C h⁻¹, $P < 0.03$), and strong as well for DPG (-0.29 ± 0.03 °C h⁻¹, $P < 0.0001$). The increase in

core body temperature after getting up was not significantly accelerated by artificial dawn (β_4 estimate = 0.003 ± 0.007 °C h⁻¹, $P = 0.68$).

Awakening cortisol response

Cortisol concentration 1 min after the alarm did not differ significantly between the control and artificial dawn condition (control: 10.4 ± 1.3 nmol L⁻¹; dawn: 12.1 ± 1.5 nmol L⁻¹; $t = -1.30$, NS). The concentration changed significantly over the 90 min after waking up ($F_{5,11} = 10.97$, $P = 0.001$), with the highest concentration on average 34.7 ± 1.8 min after the alarm in the control condition and 30.9 ± 2.9 min after the alarm in the artificial dawn condition (sign test, NS; Fig. 4). Artificial dawn did not affect the peak concentration (control: 24.3 ± 2.2 nmol L⁻¹; dawn: 24.5 ± 1.9 nmol L⁻¹; $t = -0.13$, NS). No significant main effect of artificial dawn ($F_{1,15} = 1.86$, NS) nor a significant artificial dawn by time interaction effect ($F_{5,11} = 1.99$, NS) was observed over the 90 min in the amount of cortisol. The main effects of artificial dawn and the interaction effects with time during the first 30 min after waking up were tested separately. This was performed based on our hypothesis that the major changes in cortisol could be expected until the peak in the awakening cortisol response was reached after approximately 30 min (see also Thorn *et al.*, 2004). No significant effects of artificial dawn on cortisol during the first 30 min were found (main effect: $F_{1,15} = 2.12$, NS; interaction: $F_{2,14} = 1.82$, NS).

Sleep EEG

No significant differences between both conditions were found in the percentages of each sleep stage during the last 30 min prior to the audible alarm (Table 1). A non-significant trend towards more wakefulness was seen in the artificial dawn condition compared with control ($Z = -1.81$, $P = 0.07$). Sleep efficiency (percentages of stages 2 + 3 + 4 + REM in the 30 min) was 78.1 ± 4.7 and $69.8 \pm 4.8\%$ in the control and the artificial dawn conditions, respectively ($Z = -1.57$, NS).

From the EEG recordings, the onset time of the first arousal after the start of artificial dawn and the onset time of the last arousal not followed by sleep was scored. An arousal was defined as a switch to either wakefulness, stage 1 or movement time. The timing of the last arousal without subsequent sleep, by definition, is wake up time. The first arousal within the 30 min prior to the audible alarm occurred on average 6.5 ± 1.8 min and 7.7 ± 1.9 min after the start of the 30-min period in the control and artificial dawn conditions, respectively ($Z = -0.41$, NS). In the artificial dawn condition, this corresponded with a light intensity of 1.8 lux measured at the pillow, facing the Wake-up Light. Between 5 and 10 min after the start of the 30-min period, the accumulation of wakefulness started to differ between conditions. In this period, light intensity in the experimental condition increased from 0.4 to 4.5 lux. Only between 10.5 and 14.5 min after the

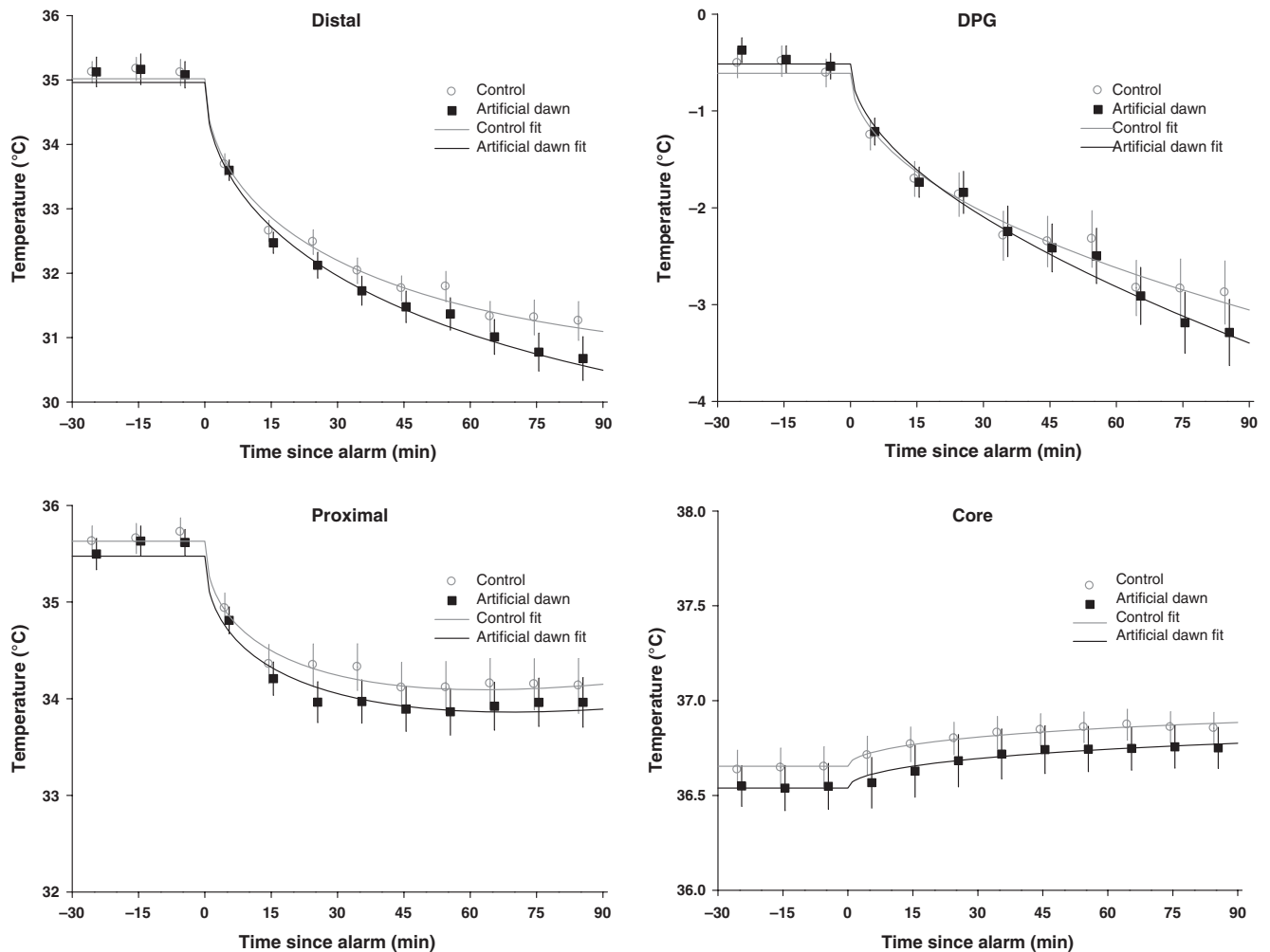


Figure 3. Average (\pm SEM) patterns of distal and proximal skin temperatures, of distal-to-proximal skin temperature gradient (DPG), and of core body temperature starting 30 min prior to the audible alarm (at 0) until 90 min after the alarm in the control (circles, open symbols) and the artificial dawn (squares, closed symbols) conditions. The lines represent the best-fitted curve through the data points ($n = 15$).

start of the 30-min period the cumulative amount of arousals in the artificial dawn condition reached significance compared with the control condition (two-tailed P -values between 0.04 and 0.09). The light intensity increased during this period from 5.4 to 17.8 lux. Most subjects fell asleep again after short periods of wakefulness between 10.5 and 14.5 min after the start of dawn. The final wake up time differed significantly between conditions ($Z = -2.59$, $P = 0.01$), but the difference was small: 2.2 ± 0.9 min before the alarm in the control; and 4.7 ± 1.1 min before the alarm in the artificial dawn condition (Fig. 5).

Sleep stage on final awakening did not differ between conditions (control: eight subjects REM sleep and eight subjects Stage 2; artificial dawn: seven subjects REM sleep and nine subjects Stage 2 (chi-square, NS).

Parameters explaining subjective ratings

To test what physiological parameters contributed to the significant differences in sleepiness and activation between the

artificial dawn condition and the control condition, a mixed effect multiple regression analysis was performed (see Section 'Materials and methods' for procedure).

Sleepiness could best be explained by the following model:

$$\text{Sleepiness}_{ijk} = \beta_{0ijk} + \beta_1 \times \text{Distal temperature}_{ijk} + \beta_2 \times \text{Wakefulness}_{ijk} + \beta_3 \times \text{Sqrt(tpost)}_{ijk}.$$

Sleepiness was positively related to momentary distal skin temperature (β_1 estimate = 0.31 ± 0.10 unit of sleepiness $^{\circ}\text{C}^{-1}$, $P < 0.01$); negatively to the amount of wakefulness in the half hour prior to the alarm (β_2 estimate = -0.16 ± 0.05 unit of sleepiness min^{-1} , $P < 0.01$); and to sqrt(tpost) (-0.14 ± 0.05 unit of sleepiness min^{-1} , $P < 0.01$).

Activation could best be explained by the following model equation:

$$\text{Activation}_{ijk} = \beta_{0ijk} + \beta_1 \times \text{Distal temperature}_{ijk} + \beta_2 \times \text{Wakefulness}_{ijk} + \beta_3 \times \text{Cortisol}_{ijk}.$$

Activation was negatively related to the momentary distal skin temperature (β_1 estimate = -1.77 ± 0.13 unit of

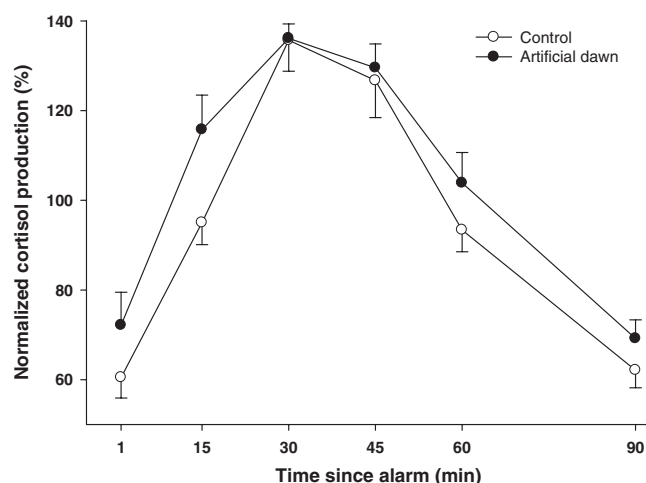


Figure 4. The average (\pm SEM) course of cortisol during the control (open symbols) and artificial dawn (closed symbols) conditions at 1, 15, 30, 45, 60, and 90 min after the alarm. Cortisol levels were normalized with respect to the average cortisol level (of both conditions) of each subject ($n = 16$).

Sleep stage (%)	Control	Artificial dawn	Z	P
Stage 1	10.3 \pm 2.2	12.3 \pm 3.1	-0.57	NS
Stage 2	36.5 \pm 8.4	40.5 \pm 10.1	-0.17	NS
Stage 3	0.1 \pm 0.1	0.1 \pm 0.0	0.00	NS
Stage 4	1.4 \pm 1.4	0.0 \pm 0.0	-1.00	NS
Wakefulness	10.3 \pm 3.9	16.7 \pm 4.2	-1.81	0.07
REM sleep	40.2 \pm 9.0	29.2 \pm 7.3	-0.83	NS
Movement time	1.3 \pm 0.4	1.3 \pm 0.3	0.00	NS

NS, not significant; REM, rapid eye movement.

activation $^{\circ}\text{C}^{-1}$, $P < 0.01$) and to the momentary cortisol concentration (-0.07 ± 0.04 unit of activation per nmol L^{-1} , $P < 0.05$), and positively related to amount of wakefulness prior to waking up (0.50 ± 0.15 unit of activation min^{-1} , $P < 0.01$).

DISCUSSION

In this study, we confirmed that sleep inertia (subjective ratings on sleepiness and activation, and performance) is most severe immediately after waking up and decreases during the following 90 min (Achermann *et al.*, 1995; Jewett *et al.*, 1999; Wertz *et al.*, 2006). When exposed to 30 min of artificial dawn prior to the alarm, subjects felt less sleepy and more active during the 90 min after waking up compared with the 90 min in the control condition. These differences between conditions in sleepiness and activation scores were not apparent in the first minute after waking up. This may be due to either statistical power or indicate a fundamental property of the waking up

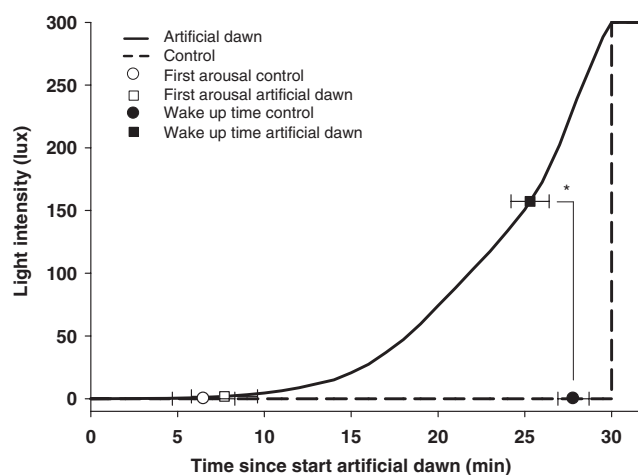


Figure 5. Rise in light intensity (lux) of the Wake-up Light (solid line) starting 30 min prior to the audible alarm (at 30). In the control condition (dashed line) the light was switched on at the audible alarm. Mean (\pm SEM) first arousal in the control (white circle) and the artificial dawn (white square), and mean (\pm SEM) wake up time in the control (black circle) and the artificial dawn (black square).

process itself. Obviously the repeatedly lower sleepiness and higher activation values during the 90-min waking period after artificial dawn compared with the same period in the control condition resulted in a significant main effect, but the variance in the data could be too high and the number of subjects too low to be able to find a significant difference at only one time point (immediately after waking up). On the contrary, 'the waking up process' may take some time and may only become apparent after waking up.

For the purpose of the study, subjects were selected who substantially suffer from sleep inertia. They reported to require more than 1 h before feeling fully awake on workdays (Roenneberg *et al.*, 2003). Chronotype evaluations (Zavada *et al.*, 2005) revealed that late chronotypes are overrepresented in the sample of selected subjects, and that their sleep on workdays is much earlier than on free days. MSF, as obtained by the MCTQ, has been shown to correlate to Morningness–Eveningness Questionnaire (MEQ) scores (Zavada *et al.*, 2005), and both midsleep time and MEQ score have been shown to correlate to dim-light melatonin onset (Martin and Eastman, 2002) and to other physiological circadian phase markers like body temperature and cortisol (Bailey and Heitkemper, 2001). Subjects within the present study differed in circadian phase as determined by their MSF corrected for sleep deficits accumulated over the workweek (MSFsc; Roenneberg *et al.*, 2007). The start of artificial dawn and waking up time was in accordance to habitual wake up time on workdays. Because of these reasons, there was some interindividual difference in circadian timing of artificial dawn exposure and waking up. The phase angle between MSFsc and start of artificial dawn and subsequent waking up could, however, not explain sleep inertia severity; neither did it explain the effect of artificial dawn. This is interesting because circadian phase is a major factor for the non-visual effects of

light exposure. It suggests that the artificial dawn in this study does not necessarily interact with the underlying circadian system but rather has an acute effect upon physiological processes around the moment of waking up irrespective of its timing within the present (narrow) range of circadian phases. In this study, it is shown that changes in skin blood flow and associated changes in skin temperature parallel the sleep inertia process; similar to how these thermoregulatory processes are correlated to the evening increase of sleepiness and the initiation of sleep after lights off in the evening. Sleep is typically initiated when heat loss is maximal and usually occurs during the circadian peak of skin temperature (Kräuchi, 2007; Van Someren, 2004), that is the major cause of the nocturnal decline in core body temperature rhythm (Campbell and Broughton, 1994; Kräuchi, 2007; Van Someren *et al.*, 2002; Zulley *et al.*, 1981). In the morning, the opposite occurs when heat production is dominant over heat loss, resulting in an increase in core body temperature (Kräuchi, 2007). In this study, subjects changed from supine to upright position after waking up. This has caused strong masking effects in body temperature on top of the waking up process during both the control and artificial dawn conditions. Nevertheless, artificial dawn prior to waking up did result in an accelerated decline in distal and proximal skin temperatures after getting up, which was also reflected in an accelerated decline in the DPG. This suggests that vasoconstriction of skin blood vessels develops faster after being exposed to artificial dawn prior to waking up compared with the control condition. This could be explained by direct activation of the sympathetic nervous system by light (Saito *et al.*, 1996; Scheer *et al.*, 1999).

Fluctuations in distal skin temperature are always larger than fluctuations in proximal skin temperature (Kräuchi, 2007). Therefore, it is not surprising that in this study the absolute effect of artificial dawn is larger in distal skin than proximal skin regions. Another explanation could be that artificial dawn interacts with the peripheral vasoconstriction caused by the change in body position and that this effect is stronger in distal skin regions.

During the 30 min of artificial dawn, there is little difference in visually scored sleep stages compared with the last 30 min of sleep in the control condition. The average timing of the first arousal (either wakefulness, stage 1 or movement time) did not differ between the artificial dawn and control condition. Therefore, the relatively low light intensity in the artificial dawn condition during the first 10 min, in which these arousals occurred, did not wake up the subjects. However, during the following 5 min the accumulation of arousals was steeper in the artificial dawn condition than in the control condition. This period also coincides with a substantial increase in light intensity (from 5.4 to 17.8 lux). Short arousals (periods of artifacts over EMG + EEG) occur regularly during the whole sleep period (Dijk *et al.*, 1987; Gordijn *et al.*, 1999), and most of them are not noticed by the person at all. Only some appear to be associated with conscious awareness of being awake. It is not known whether subjects were consciously aware of the light during an arousal and whether this has contributed to the

observed changes after waking up. By asking the subjects afterwards, they reported to have noticed the difference between the artificial dawn and control conditions. It is also unknown whether subjects opened their eyes during an arousal. Only about 5% of light intensity comes through the eyelids (Ando and Kripke, 1996), and if subjects opened their eyes they were thus exposed to a much higher light intensity.

Abrupt awakenings are reported to worsen sleep inertia complaints (Dinges, 1990; Dinges *et al.*, 1981). A gradual way of waking up, induced by artificial dawn, could thus reduce sleep inertia complaints.

Indeed in our regression analysis the amount of wakefulness during the 30 min prior to the alarm contributed both to the decrease in sleepiness and to the increase in activation after waking up. In addition to the amount of wakefulness prior to the alarm, the decrease in distal skin temperature after waking up contributed strongly to the model. Our data confirm the close functional relationship between the dissipation of sleepiness and skin temperature, as was previously reported in relation to DPG (Kräuchi *et al.*, 2004). It is interesting that in our study distal skin temperature rather than DPG or proximal skin temperature added significantly to the model explaining sleepiness. Little is known about the association of the regulation of skin blood flow and the regulation of alertness upon waking up from sleep. Typically, a 10-min nap does not induce the adverse effects of sleep inertia upon awakening, and this may be because of insufficient time for thermoregulatory changes to occur (Brooks and Lack, 2006). Further experiments are required to determine whether skin temperature changes after waking up and the dissipation of sleep inertia are causally related, as has been shown to be feasible using mild skin temperature manipulation while obtaining objective vigilance measures during daytime (Fronczek *et al.*, 2008; Raymann and Van Someren, 2007). This study is the first to show that manipulation of sleep inertia by artificial dawn coincides with effects on skin temperature.

Interestingly, but also unexpectedly, the effect of the awakening cortisol response as included in the model on activation appeared to be negative. This negative relationship suggests that an increased awakening cortisol response has a detrimental effect on the dissipation of sleep inertia. The exact function of the awakening cortisol response is as yet unknown. Although cortisol does show consistent responses to stress (Kemeny, 2003), the morning increase in cortisol was not associated to any detectable psychological stress in our study. Previously, light after waking up has been shown to increase cortisol production (Scheer and Buijs, 1999), and one study showed a significantly higher awakening cortisol response with the use of a dawn waking up system (Thorn *et al.*, 2004). In this study, we did not find an effect of the dawn signal on cortisol. The discrepancy between our study and the study of Thorn *et al.* (2004) can be explained by differences between the control conditions used in both experiments. In the study of Thorn *et al.* (2004) artificial dawn was tested against a normal alarm clock (with no light). In our study light was turned on in

the control condition, together with the audible alarm at waking up. This was performed to test whether dawn itself, and not the light exposure after waking up, induced a reduction of sleep inertia and an increase in cortisol. It is possible that the light exposure immediately after the alarm in both conditions may have increased cortisol to such an extent that a possible additional effect of artificial dawn on cortisol could not be detected.

CONCLUSION

People who require a large amount of time after awakening before feeling fully alert can reduce their symptoms of sleep inertia and the time until feeling fully awake by exposing themselves to an artificial dawn signal. Skin temperatures showed an accelerated decline after awakening in the artificial dawn condition. A multiple regression analysis revealed that the physiological background explaining the positive effects of artificial dawn on the dissipation of sleep inertia involves light sleep and an accelerated distal skin temperature decline after awakening.

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